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09/801,968	03/07/2001	Nobuyuki Itoh	60219-4/PP-17150.001	8729

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EXAMINER

SAOUD, CHRISTINE J

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/801,968

Applicant(s)

ITOH ET AL.

Examiner

Christine J. Saoud

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on RCE filed 11 April 2005.  
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-65 is/are pending in the application.  
4a) Of the above claim(s) 1-11, 19-21 and 23-60 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 12-18, 22 and 61-65 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☒ The drawing(s) filed on 21 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 21 March 2005 has been entered.

### ***Response to Amendment***

Claims 12-18 have been amended in the response filed 21 March 2005. Claims 1-65 are pending in the instant application. Claims 1-11, 19-21, and 23-60 stand with drawn and claims 12-18, 22 and 61-65 are under examination in the instant Office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 21 March 2005 have been fully considered but they are not deemed to be persuasive.

***Non-compliance with 37 CFR 1.121***

The claims filed 21 March 2005 are not in compliance with 37 CFR 1.121 for the following reasons.

Claim 14 is indicated to be "(Previously Amended)". This is not consistent with the underlining in the claim. Secondly, the identifier "Previously Amended" is not one of the identifiers indicated in 37 CFR 1.121 (c).

Claims 61-65 are indicated to be "(Previously Added)". This identifier is not one of the permitted identifiers listed in 37 CFR 1.121(c). These claims should be referred to as (Previously Presented).

Any subsequent amendment that fails to comply with 37 CFR 1.121 will be held as non-responsive.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 22 and 61-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 12 has been amended to recite "wherein said biological activity is defined as the ability of said isolated polypeptide to lower serum phosphate levels in a mouse administered with said isolated polypeptide, and wherein said administered polypeptide is non-cleavable between amino acid positions 176 and 179 during expression". The instant specification has no basis for such a limitation, and therefore, this is new matter. Claims 22 and 61-65 depend from claim 12, and are therefore, also rejected for new matter.

***Claim Rejections - 35 USC § 101***

Claims 12-18, 22 and 61-65 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for the reasons of record in the previous Office actions.

Applicant argues the rejection and points to page 7 of the specification which cites "and incorporates by reference, Nature Genetics 26: 354-358 (2000) "which discusses disorders of phosphate metabolism". However, it is not clear that the publication was ever meant to be incorporated by reference because there is no positive statement of such at the point the publication is mentioned. Furthermore, the incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously

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incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Secondly, the specification never provides a specific and substantial utility for the claimed invention. Rather, the specification at page 7 states that the claimed protein, FGF-23, can be cleaved during expression resulting in a 20kDa protein and a 7-12 kDa protein as well as a noncleaved expression product of 28 kDa. The specification suggests that cleavage may play a role in disorders of phosphate metabolism and cites the Nature Genetics publication. At page 8 of the specification, it is stated that “[t]he invention provides compositions and methods for treating disorders of phosphate metabolism, wherein the disorder is a result of cleavage of FGF-23. The composition can comprise an FGF-23, or a polynucleotide encoding FGF-23, wherein the FGF-23 has been mutated to alter or delete the cleavage site.”. However, there are no disorders identified in the instant specification which are the result of cleavage of FGF-23. This disclosure is inadequate to provide utility for the claimed invention, because it is not specific for how the invention is to be used. The art teaches that if the FGF-23 protein is mutated such that cleavage does not occur, then the disease that occurs is hypophosphataemic rickets. Therefore, without further experimentation on the invention being claimed, one of ordinary skill in the art would not have been able to use the invention in a real world manner. Applicant’s disclosure of how to use the claimed invention is contrary to the way the invention actually works in nature, absent evidence to the contrary.

Applicant again cites the Kavanaugh Declaration to support a disclosure of utility in the instant application. However, the information that non-cleavable FGF-23 lowers phosphate levels is not disclosed in the instant specification. There is no disclosure of how FGF-23 or non-cleavable FGF-23 would modulate phosphate levels, and therefore the suggestion that the protein could be used for treatment of phosphate disorders is an invitation to experiment as well as a non-specific utility. This is because each form of the protein will only modulate phosphate in one direction, and not both directions, therefore, the disclosure is not specific. The disclosure is also not substantial because the asserted utility does not provide a specific benefit to the public in a currently available form since both forms of the protein would need to be tested before they could be used to either increase or decrease phosphate metabolism.

With regard to Applicant's reliance on the Nature Genetics disclosure and the link of FGF-23 gene mutations to hypophosphataemic rickets, this paper was published in November 2000. Applicant did not disclose this information of the assertion that FGF-23 was associated with phosphate metabolism until December 2000 in provisional application 60/251,650. Therefore, this reference is available as prior art (see rejections below).

Applicant asserts at page 15 of the response that they have identified a mechanism by which FGF-23 is associated with phosphate metabolism. However, this information was not available at the time the instant application was filed. Utility must be established at the time the instant application was filed, and not discovered after the fact. There is no evidence in the instant specification as originally filed that non-

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cleavable FGF-23 lowers serum phosphate levels. In fact, the specification suggests that it is the cleavable form of the protein that is associated with the disease state, which is not the case as evidenced by the references cited by Applicant. Therefore, at the time the instant application was filed, there was no disclosure of a specific, substantial and credible utility for the claimed invention and the rejection is maintained.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 12-18 and 61-65 are rejected under 35 U.S.C. 102(a) as being anticipated by The ADHR Consortium (Nature Genetics 26: 345-348, 2000).

The ADHR Consortium discloses a protein which is identical to SEQ ID NO:4 of the claims (see Figure 3). Furthermore, mutations at positions 176 and 179 are identified (see Figure 3 legend). Therefore, the claims are anticipated by the reference.

Claims 12-18, 22 and 61-65 are rejected under 35 U.S.C. 102(e) as being anticipated by Econs et al. (Pregrant publication 20020156001).



Econs et al. disclose a protein which is 100% identical to that of SEQ ID NO:4. Econs et al. disclose mutations at positions 176 and 179 of the protein as well as pharmaceutical compositions of the protein. Therefore, the claims are anticipated by the prior art.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on mttr, 8:00-2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**CHRISTINE J. SAOUD  
PRIMARY EXAMINER**

*Christine J. Saoud*